

[ P O S T - H O C A N A L Y S I S ]

# A Four-question Approach to Determining the Impact of Acne Treatment on Quality of Life

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## ABSTRACT

Facial acne vulgaris can have profound effects on health-related quality of life. In some studies, patients with acne vulgaris reported results similar to those noted with other chronic diseases, such as asthma, arthritis, or diabetes. Clinical objective assessments alone do not adequately capture the impact of acne vulgaris severity from a patient's perspective. Health-related quality-of-life assessment is important in order to fully characterize the overall burden of disease and effectiveness of treatment as the perspectives of the patient are also taken into account. Previous studies of the impact of acne vulgaris treatment on health-related quality of life have been limited in their scope of assessment. Drawbacks of prior studies have included small numbers of patients, health-related quality-of-life parameters that were not adequately evaluated, inclusion of only a limited range of mild-to-moderate acne vulgaris severity, or being unblinded or observational in study design. The Acne Quality of Life is an acne-specific questionnaire developed to assess treatment impact on the health-related quality of life of patients with acne vulgaris. Its psychometric properties and degree of responsiveness are well-established. Improvement in Acne Quality of Life with the fixed combination clindamycin phosphate 1.2%/benzoyl peroxide 2.5% aqueous gel in the largest cohort of acne vulgaris patients where health-related quality of life was studied has been reported recently. Significant improvements in all four domains over 12 weeks were seen with clindamycin phosphate 1.2%/benzoyl peroxide 2.5% aqueous gel compared to patients treated with individual active ingredients or vehicle ( $p < 0.001$ ). Length and time required for completion of the 19-item Acne Quality of Life questionnaire is likely to preclude its use in clinical practice. A condensed, validated Acne Q-4 scale based on the four items most broadly representative of health-related quality of life combined with a high level of correlation to the Acne Quality of Life questionnaire has been suggested as a more realistic approach that may be applied by clinicians when managing patients with acne vulgaris. The authors present data on the effectiveness of clindamycin phosphate 1.2%/benzoyl peroxide 2.5% aqueous gel on health-related quality of life based on this Acne Q-4 scale. (*J Clin Aesthet Dermatol.* 2012;5(3):51–57.)

Acne vulgaris (AV) is frequently localized to the face and trunk affecting appearance and resulting in a range of psychosocial impacts including anxiety and depression, social withdrawal, and lack of self-confidence.<sup>1–5</sup> These negative impacts are often the primary motivation for patients with AV to seek treatment.<sup>5</sup> The impact of facial AV on health-related quality of life (HRQL) can be profound and similar to that reported by patients with other chronic diseases, such as asthma, arthritis, or diabetes.<sup>6</sup> Evaluation of AV using only clinical objective assessments, such as lesion counts and physician-grading classifications, does not

adequately capture the impact of AV from the perspective of the patient.<sup>7</sup> Assessment of impact on HRQL is needed in order to fully characterize the overall disease burden and effectiveness of treatment.

Instruments to assess HRQL should be reliable and responsive and developed based on patient input on relevant and important aspects related to the disease under study.<sup>8–10</sup> A number of acne-specific psychometric instruments have been developed, including the Assessment of the Psychological and Social Effects of Acne (APSEA), the Acne Disability Index (ADI), the Cardiff Acne Disability Index

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TABLE 1. Acne-QoL items and domains

SELF-PERCEPTION	ROLE-EMOTIONAL	ROLE-SOCIAL	ACNE SYMPTOMS
How unattractive did you feel?	How upset were you about having facial acne?	How concerned or worried were you about meeting new people?	How many bumps did you have on your face?
How embarrassed did you feel?	How annoyed did you feel at having to spend time everyday cleaning and treating your face?	How concerned or worried were you about going out in public?	How many bumps full of pus did you have on your face?
How self-conscious (uneasy about oneself) did you feel?	How concerned or worried were you about not looking your best?	How much was socializing with people a problem for you?	How much scabbing from facial acne?
How dissatisfied with your appearance did you feel?	How concerned or worried were you that your acne medication/ products were working fast enough in clearing up the acne on your face?	How much was interacting with the opposite sex (or same sex if gay or lesbian) a problem for you?	How concerned or worried were you about scarring?
How much was your self confidence (sure of yourself) negatively affected?	How bothered did you feel about the need to always have medication or cover-up available for the acne on your face?		How oily was your facial skin?

(CADI), the Acne Quality of Life Scale (AQOL), and the Acne Quality of Life (Acne-QoL).<sup>4,11–14</sup> The Acne-QoL was developed specifically to assess HRQL for clinical trials of AV. Its validation involved extensive subject interviews to assist in item generation, item reduction, and pilot testing.<sup>14</sup> Psychometric evaluation demonstrated it to be reliable, valid, and responsive.<sup>15,16</sup> Unfortunately, their narrow range of assessment has limited previous studies designed to evaluate the impact of AV treatment on HRQL. Among these limitations are the inclusion of small patient numbers, inadequate assessment of some important HRQL parameters, inclusion of only mild-to-moderate AV severity, or use of an unblinded or observational study design.<sup>2,4,6,13–15,17–20</sup>

One of the largest studies of patients with AV to date evaluated the efficacy and tolerability of a fixed-combination of clindamycin phosphate 1.2%/benzoyl peroxide 2.5% aqueous gel (Clin 1.2%/BP 2.5% AqG) in moderate-to-severe AV and incorporated the Acne-QoL instrument. Clinical

results and impact of Clin 1.2%/BP 2.5% AqG on HRQL have been reported elsewhere.<sup>21,22</sup> Clin 1.2%/BP 2.5% AqG was significantly superior to all three monad study arms (each individual active ingredient and vehicle) in reducing the number of inflammatory and comedonal AV lesions, and significantly improved HRQL across all four domains of the Acne-QoL questionnaire (acne symptoms, role-emotional, self-perception, role-social)(all  $P < 0.001$ ). Overall, the safety and tolerability of Clin 1.2%/BP 2.5% AqG were comparable to its active ingredients and vehicle.<sup>21</sup>

Pitfalls of the Acne-QoL instrument include its length, lack of a validated aggregate or total score, and its application exclusively to facial AV. In addition, time taken to complete the 19-item Acne-QoL questionnaire (approximately 5–7 minutes) would likely preclude its use in routine clinical practice.<sup>14</sup> Here, the impact of AV on HRQL has largely been based on clinical impression rather than a formalized method of inquiry.<sup>23</sup> A condensed version with a shorter completion

TABLE 2. Composition of four-item condensation of Acne QoL

	DOMAIN-DEPENDENT REGRESSION	DOMAIN-INDEPENDENT REGRESSION	DOMAIN-RANKED	PATIENT-RANKED
SELF-PERCEPTION	How unattractive did you feel?	How dissatisfied with your appearance did you feel?	How self-conscious (uneasy about oneself) did you feel?	How dissatisfied with your appearance did you feel?
ROLE-EMOTIONAL	How concerned or worried were you about not looking your best?	How concerned or worried were you that your acne medication/products were working fast enough in clearing up the acne on your face?	How concerned or worried were you about not looking your best?	How upset were you about having facial acne?
ROLE-SOCIAL	How concerned or worried were you about going out in public?	How concerned or worried were you about going out in public?	How concerned or worried were you about meeting new people?	How concerned or worried were you about meeting new people?
ACNE SYMPTOMS	How many bumps full of pus did you have on your face?	How many bumps full of pus did you have on your face?	How much scabbing from facial acne?	How concerned or worried were you about scarring?

time may be more practical and clinically relevant for use in the ambulatory dermatology clinic setting. Since many of the items in the Acne-QoL appear redundant, condensing the number of items from the 19 used for the large-scale survey to four clinically purposeful items with one item targeted from each domain should reduce completion time while maintaining the validity of the construct. This condensed scale (Acne-Q4) has been shown to be a good predictor of the Acne-QoL total score.<sup>24</sup>

The purpose of this *post-hoc* study was to re-analyze the original HRQL data from the pivotal studies using this Acne-Q4 scale to provide additional insights into the impact of Clin 1.2%/BP 2.5% AqG on HRQL.

## METHODS

**Data source.** The data for the present analysis were collected in two identical, double-blind, randomized, placebo-controlled, pivotal studies assessing the safety and

efficacy of Clin 1.2%/BP 2.5% AqG for the treatment of moderate-to-severe facial AV in 2,813 patients (n=1414 in Study A and n=1399 in Study B) 12 years of age or older. Patients were stratified by Fitzpatrick skin type and randomized into one of the following four treatment groups: Clin 1.2%/BP 2.5% AqG, clindamycin phosphate 1.2% gel, benzoyl peroxide 2.5% gel, or vehicle gel. All patients applied the study medication once daily for 12 weeks. Full details of the methodology of these pivotal trials and results are described in detail elsewhere.<sup>21</sup> The data from the two trials were pooled for the present analyses because there were no differences in study design, no meaningful differences in the study populations, and the efficacy and safety results were similar in both trials. Both studies received approval by Institutional Review Boards prior to subject enrollment and were conducted in accordance with the Declaration of Helsinki.

**Measures.** The Acne-QoL is a facial acne-specific

TABLE 3. Subject demographics and baseline characteristics by treatment group

ANALYSIS OF SUBJECT DEMOGRAPHIC AND BASELINE CHARACTERISTICS		
	CLINDAMYCIN PHOSPHATE 1.2%- BPO 2.5% N=797	VEHICLE  N=395
AGE (YEARS)		
Mean	19.2	19.4
Median	16.8	16.7
Range	12.1–54.7	12.2–50.9
GENDER		
Male	389 (48.8%)	203 (51.4%)
Female	408 (51.2%)	192 (48.6%)
ETHNICITY		
Hispanic/Latino	124 (15.6%)	61 (15.4%)
Not Hispanic/Latino	673 (84.4%)	334 (84.6%)
RACE		
Caucasian	618 (77.5%)	305 (77.2%)
African American	128 (16.1%)	68 (17.2%)
Native Hawaiian/Pacific Islander	3 (0.4%)	2 (0.5%)
Asian	17 (2.1%)	11 (2.8%)
American Indian/Alaska Native	5 (0.6%)	3 (0.8%)
Other	35 (4.4%)	13 (3.3%)
GLOBAL SEVERITY SCORE		
Moderate	643 (80.7%)	319 (80.8%)
Severe	154 (19.3%)	76 (19.2%)
INFLAMMATORY LESION COUNT (MEDIAN)	26.4	26.1
NONINFLAMMATORY LESION COUNT (MEDIAN)	47.4	44.0
TOTAL LESION COUNT (MEDIAN)	73.8	70.2

psychometric instrument comprising 19 items within four domains (self-perception, role-emotional, role-social, acne symptoms) (Table 1). Each item within a domain is scored from 0 to 6 based on response selections ranging from extremely (or extensive) to not at all (or none). Higher scores within each domain reflect better HRQL.

The development of the Acne-Q4 (4-item index of the Acne-QoL) involved the following two steps: a construction phase and a validation phase. Of the four versions investigated (Table 2) in the construction phase, the patient-ranked version demonstrated the greatest breadth of information on HRQL and was of greatest face validity given the relative importance ranking of these items by patients. The Acne-Q4 explained 98.5 percent of the variation in total score of Acne-QoL. Validation of the Acne-Q4 resulted in Pearson correlation coefficients of 0.967. The total Acne-Q4 score was calculated by summing the mean values of each of the four questions as follows and compared between Clin 1.2%/BP 2.5% AqG and vehicle.

#### Calculation of Acne-Q4

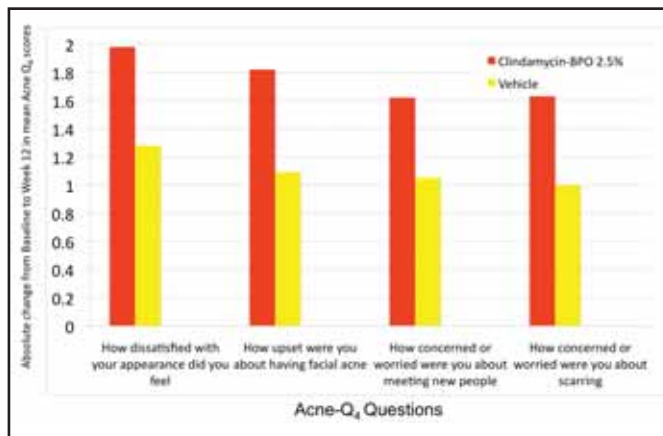
*Acne-Q4 = feeling upset + dissatisfied with appearance + concern about meeting new people + concern about scarring*

Subjects completed the Acne-QoL at Baseline and Week 12. In addition to calculating the overall Acne-Q4 score, individual questions were studied to provide additional HRQL information and comparison.

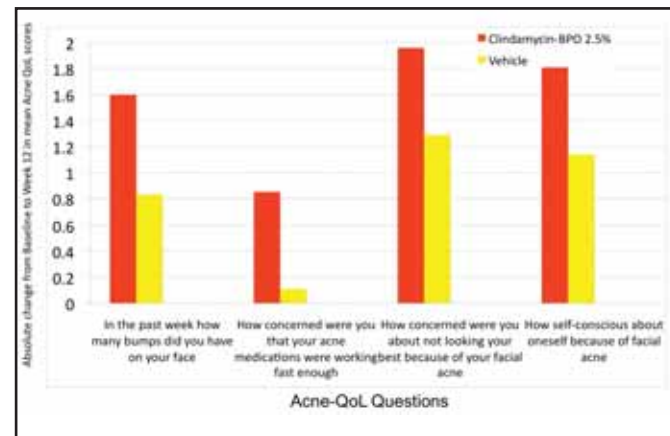
## RESULTS

**Baseline demographic and clinical characteristics.** The baseline demographic and clinical characteristics were similar across the two treatment groups (Table 3). The mean age across the treatment groups was 19.3 years and the majority of subjects were Caucasian (77.5%), there were slightly more female subjects (52.4%), and almost 1 in 5 subjects had severe acne. The mean lesion counts and Acne-QoL domain scores were similar across all of the treatment groups. Baseline Acne-QoL domains scores tended to be lower in patients who rated their AV severity as more severe at Baseline.

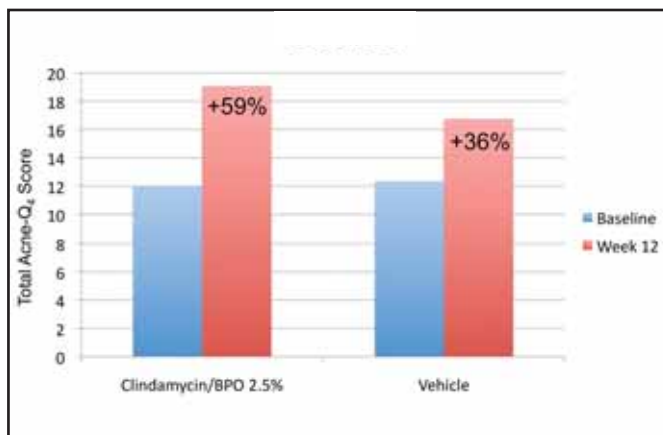
**Individual Acne-Q4 scores.** Improve-



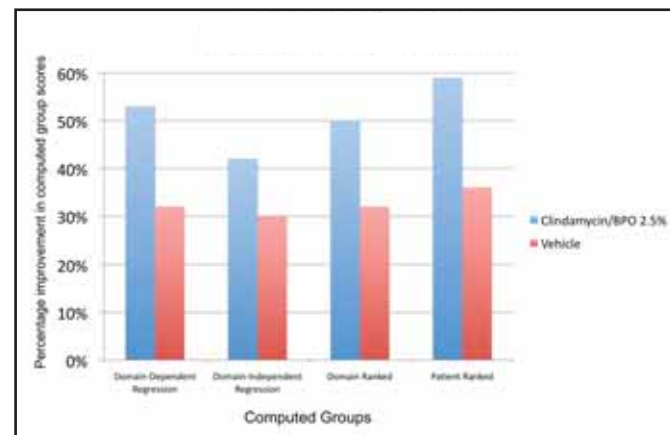
**Figure 1.** Improvement in individual Acne-Q4 scores



**Figure 2.** Improvement in individual Acne-QoL scores (greatest impact)



**Figure 3.** Improvement in Acne-Q4 scores



**Figure 4.** QoL improvement in acne computed groups

ments seen in the individual Acne-Q4 scores by Week 12 are shown in Figure 1. Clin 1.2%/BP 2.5% AqG showed a marked improvement compared to vehicle across all four questions. Additional impact on HRQL of Clin 1.2%/BP 2.5% AqG over vehicle was 0.70 ("How dissatisfied with your appearance did you feel?"), 0.73 ("How upset were you about having facial acne?"), 0.57 ("How concerned or worried were you about meeting new people?"), and 0.63 ("How concerned or worried were you about scarring?") at 12 weeks. For the majority of subjects, Clin 1.2%/BP 2.5% AqG provided an additional one-point improvement in Acne QoL score over that seen with vehicle. This translates to the answer "not at all" to the question, "In the past week, how dissatisfied were you with your appearance?" compared to "a little bit" with vehicle and "somewhat/a good bit" at Baseline. Similarly, 36 percent of subjects recorded "not at all" to the question, "In the past week, how upset were you about having acne?" after 12 weeks of Clin 1.2%/BP 2.5% AqG compared to 20 percent on vehicle. Here, subject responses at Baseline were fairly evenly distributed from "extremely" to "a little bit." The best results were seen in subjects with the lower Baseline scores.

Impact on HRQL of Clin 1.2%/BP 2.5% AqG over vehicle was comparable for a number of questions not included in the Acne-Q4 instrument: "In the past week, how many bumps did you have on your face (0.77)?" and "How concerned were you that your acne medications were working fast enough (0.74)?" "How concerned were you about not looking your best because of your facial acne (0.67)?" "How self-conscious about oneself are you because of facial acne (0.67)?" (Figure 2).

**Acne-Q4 scores.** Acne-Q4 scores were similar at Baseline between Clin 1.2%/BP 2.5% AqG (12.03) and vehicle (12.34). By Week 12, the Acne-Q4 score had increased by 59 percent Clin 1.2%/BP 2.5% AqG compared to 36 percent with vehicle (Figure 3).

**Other condensations.** Improvements seen with Clin 1.2%/BP 2.5% AqG were greatest in the patient-ranked Acne-Q4 scale compared to the other computations that were investigated (Figure 4). Replacing the two lowest scoring questions in terms of improvement with Clin 1.2%/BP 2.5% AqG by two questions showing higher absolute improvement did not increase the overall impact of Clin 1.2%/BP 2.5% AqG on HRQL.



## DISCUSSION

There was a marked improvement in Acne-Q4 score with Clin 1.2%/BP 2.5% AqG compared to vehicle by Week 12. Improvement with Clin 1.2%/BP 2.5% AqG from Baseline to Week 12 was 59 percent. This compares to 47 percent in role-emotional, 37 percent in role-social, 59 percent in self-perception, and 49 percent in acne symptoms using the traditional Acne-QoL domain scoring.

The individual items that constitute the Acne-Q4 score were selected through a process of computation that involved selecting one question from each of the domains, based on subsequent validation. The patient-ranked version revealed the greatest breadth of information on HRQL and was of greatest face validity given the relative importance ranking of these items by patients. It also showed the greatest impact of treatment with Clin 1.2%/BP 2.5% AqG on HRQL.

A limitation of the Acne-Q4 may be in the selection of one item from each domain. However, the Acne-Q4 improvement noted with Clin 1.2%/BP 2.5% AqG (59%) was comparable to that seen with its impact on "role-social" in the Acne-QoL analysis. Another alternative might be to look at those questions with the lowest baseline scores (suggesting greatest need) and the improvement seen with active treatment and vehicle. Condensing the Acne-QoL instrument to the following four questions—"How upset were you about having facial acne?" "How concerned were you about not looking your best because of your facial acne?" "How many bumps did you have on your face?" "How oily was your facial skin?"—resulted in a 65-percent improvement with Clin 1.2%/BP 2.5% AqG compared to 40 percent with vehicle.

Ultimately, the Acne-Q4 allows for a practical system to assess the impact of AV and its treatment on HRQL that can be used in clinical practice in cases where the clinician may find it to be helpful. Examples may include confirmation of the benefits of a specific treatment for third-party purposes, to provide attention in specific cases where AV is more problematic from a psychosocial standpoint, or as a tool that some providers may want to incorporate consistently in their practice to gain greater insight into how patients are personally affected by AV. The Acne-Q4 can be taught to clinical assistants to carry out with patients, and is more time-efficient than other large-scale QoL measurement tools that are used in formal clinical trials and take much more time to complete. Based on its application to the pooled data from two identical large pivotal trials evaluating a topical acne therapy (Clin 1.2%/BP 2.5% AqG once daily over 12 weeks), the outcomes provided by the Acne-Q4 reasonably reflect those obtained through using a much longer assessment tool, the Acne-QoL. Thus, the Acne-Q4 described in this article may serve as a useful measure of QoL that can be applied selectively in clinical practice.

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